News Release

Media contact:
Natalia Salomao
Mobile: +1 732-325-8306
nsaloma7@its.jnj.com

Investor contact:
Jen McIntyre
Office: +1 732-524-3922
JMcInty3@its.jnj.com

New Real-World Observational Analysis of UPTRAVI® (selexipag) Underscores the Importance of Risk Assessment for Treating Pulmonary Arterial Hypertension (PAH) Patients

Data from the SPHERE Registry published in the Journal of Heart and Lung Transplantation

SOUTH SAN FRANCISCO, CA – April 6, 2021 – Findings from an analysis of the first 500 patients enrolled in the SPHERE registry (**S**elexi**P**ag: t**H**e us**E**rs d**R**ug r**E**gistry) found more than three-quarters (76%) of pulmonary arterial hypertension (PAH) patients treated with UPTRAVI® (selexipag) either maintained (56%) or reduced (20%) their one-year mortality risk score. The SPHERE results were published in the April issue of the *Journal of Heart and Lung Transplantation (JHLT)*. SPHERE is an ongoing real-world, observational, user registry using two different risk assessment methods that describes the clinical characteristics, outcomes and dosing/titration regimens in patients with PAH who are being treated with UPTRAVI.

PAH is a rapidly progressive disease with no known cure. For individuals with PAH, risk assessment is necessary to evaluate disease progression and inform treatment decisions based on patients' prognosis.[1] UPTRAVI is an oral prostacyclin pathway agent (PPA) indicated for the treatment of patients with PAH (World Health Organization [WHO] Group I, functional class [FC] II-III) to delay disease

progression and reduce the risk of hospitalization. In the pivotal GRIPHON trial, UPTRAVI was proven to reduce the risk of disease progression by 40%.

"Within the PAH treatment paradigm, real-world evidence has become valuable information for physicians to consider when it comes to elevating the standard of care," said Nick Kim, M.D.*, primary study investigator and professor of medicine at the University of California San Diego. "Findings from the SPHERE analysis reinforce the need for physicians to be conducting routine comprehensive risk assessments and utilizing available tools such as risk calculators to ensure that PAH patients are achieving their treatment goals."

In treating patients with PAH, routine comprehensive risk assessment is strongly recommended by the 2015 European Society of Cardiology and the European Respiratory Society (ESC/ERS) Guidelines, as there is no single variable that can provide sufficient diagnostic and prognostic information. Additionally, achieving and/or maintaining a low-risk profile is a recommended adequate treatment response for patients with PAH.[2]

In the analysis of the data from the SPHERE registry, risk categories for one-year mortality are assigned to patients using two different assessments, the Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension (COMPERA) and the Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) † risk calculators, and PAH patients are classified as low, intermediate or high risk. Results from this analysis showed that at the end of the 18-month follow-up, 19.2% of patients had a lower REVEAL 2.0 risk score, 57.8% experienced no change in their REVEAL 2.0 risk score, and 20.2% noticed an increase in their REVEAL 2.0 risk score. The findings in this analysis were consistent with the COMPERA calculations as well, as 21.4% of patients experienced a positive change in their risk category (moving from a more serious to less serious category), 54.4% maintained their risk category, and 19.4% experienced a negative change in their risk category (moving from a less serious to a more serious category).

SPHERE enrolled patients who were either newly initiated on UPTRAVI (≤60 days before enrollment) or previously received UPTRAVI with documentation of dose titration at study enrollment. Data from this SPHERE analysis suggest that 87.8% of patients titrated UPTRAVI at a slower rate than 200-mcg BID increments, revealing that in the real-world environment patients were titrated less than the recommended titration schedule in the GRIPHON study. [3,4]

"We're proud to support SPHERE, as data from this registry furthers our understanding of UPTRAVI within a clinical setting in the U.S.," said Siân Walker [‡], Head of Medical Affairs, Janssen U.S., Pulmonary Hypertension. "These findings add to the growing body of evidence that demonstrates the need for utilizing risk assessment tools in clinical practice that may optimize the standard of care for patients with PAH."

Data from SPHERE are limited to what is collected during routine clinical visits, and patients are observed for up to 18 months after enrollment. In this cohort, 94.8% of patients have PAH (WHO Group I), most commonly idiopathic (49.2%) followed by connective tissue disease (CTD)-associated PAH (26.4%). 31.0% and 49.6% of patients have WHO FC II and WHO FC III disease at baseline respectively. There were no new safety signals identified with UPTRAVI in the real-world setting, and the incidence of discontinuation due to UPTRAVI treatment-related adverse events (AEs) remained low in the SPHERE analysis (7.2%). The most common AEs leading to discontinuation were headache (6.5%) and diarrhea (5.1%) in newly initiated patients, and worsening PAH (3.3%) and right ventricular failure (1.9%) in previously initiated patients.

To read the full manuscript and learn more about the SPHERE analysis, please visit https://www.jhltonline.org/article/S1053-2498(21)00018-8/fulltext.

Real-World Data Limitations

Real-world data have the potential to supplement randomized controlled trial data by providing additional information as to how a medicine performs in routine clinical practice. There are limitations, however, and real-world data cannot be used as stand-alone evidence to validate the efficacy or safety of a treatment.

About UPTRAVI® (selexipag) and the GRIPHON Trial

UPTRAVI is an oral selective prostacyclin IP receptor agonist for the treatment of PAH. UPTRAVI is the only globally available oral treatment that works on the prostacyclin pathway with evidence of long-term outcomes. UPTRAVI is available for the treatment of patients with PAH (WHO Group I, FC II-III) in more than 40 countries. In the US, UPTRAVI is indicated for the treatment of PAH to delay disease progression and reduce the risk of PAH-related hospitalization.[2] In Europe, UPTRAVI is indicated for the long-term treatment of PAH in adult patients with WHO FC II–III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 inhibitor (PDE-5), or as monotherapy in patients who are not candidates for these therapies.

The efficacy of UPTRAVI in PAH was established in GRIPHON (Prostacyclin [P**G**I2] **R**eceptor agonist **I**n **P**ulmonary arterial **H**ypertensi**ON**), the largest randomized, controlled trial ever conducted in PAH patients. The GRIPHON trial was the first multicenter, long-term, double-blind, placebo-controlled, parallel-group, event-driven Phase 3 study in patients with symptomatic PAH (N=1156; nearly all WHO FC II-III at baseline) evaluating the effects of UPTRAVI (n=574) vs placebo (n=582) targeting the prostacyclin pathway (median duration of exposure 1.4 years, up to 4.2 years). UPTRAVI was shown to delay disease progression and reduce the risk of hospitalization compared with placebo.[3] Overall, the most common AEs in the UPTRAVI group were consistent with the known side effects of prostacyclin, including headache, diarrhea, nausea, and jaw pain.[3]

[*]Dr. Nick Kim has received research support from Janssen and has served as a paid consultant to the company.

[†]The REVEAL Registry™ is a registered trademark of Actelion Pharmaceuticals Ltd.

[‡]Siân Walker Peasegood is an employee of Actelion Pharmaceuticals US, Inc.

IMPORTANT SAFETY INFORMATION

INDICATION

UPTRAVI® (selexipag) is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms.

Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), and PAH associated with congenital heart disease with repaired shunts (10%).

CONTRAINDICATIONS

Concomitant use of strong inhibitors of CYP2C8 (eg, gemfibrozil) with UPTRAVI is contraindicated.

WARNINGS AND PRECAUTIONS

Pulmonary Veno-Occlusive Disease (PVOD)

Should signs of pulmonary edema occur, consider the possibility of associated PVOD. If confirmed, discontinue UPTRAVI.

ADVERSE REACTIONS

Adverse reactions more frequent compared to placebo (≥3%) are headache (65% vs 32%), diarrhea (42% vs 18%), jaw pain (26% vs 6%), nausea (33% vs 18%), myalgia (16% vs 6%), vomiting (18% vs 9%), pain in extremity (17% vs 8%), flushing (12% vs 5%), arthralgia (11% vs 8%), anemia (8% vs 5%), decreased appetite (6% vs 3%), and rash (11% vs 8%).

These adverse reactions are more frequent during the dose titration phase.

Hyperthyroidism was observed in 1% (n=8) of patients on UPTRAVI and in none of the patients on placebo.

DRUG INTERACTIONS

CYP2C8 Inhibitors

Concomitant administration with gemfibrozil, a strong inhibitor of CYP2C8, doubled exposure to selexipag and increased exposure to the active metabolite by approximately 11-fold. Concomitant use of UPTRAVI with strong inhibitors of CYP2C8 is contraindicated.

Concomitant administration of UPTRAVI with clopidogrel, a moderate inhibitor of CYP2C8, had no relevant effect on the exposure to selexipag and increased the exposure to the active metabolite by approximately 2.7-fold. Reduce the dosing of UPTRAVI to once daily in patients on a moderate CYP2C8 inhibitor.

CYP2C8 Inducers

Concomitant administration with an inducer of CYP2C8 and UGT 1A3 and 2B7 enzymes (rifampin) halved exposure to the active metabolite. Increase UPTRAVI dose, up to twice, when co-administered with rifampin. Reduce UPTRAVI when rifampin is stopped.

DOSAGE AND ADMINISTRATION

Recommended Dosage

Recommended starting dose is 200 mcg twice daily. Tolerability may be improved when taken with food. Increase by 200 mcg twice daily, usually at weekly intervals, to the highest tolerated dose up to 1600 mcg twice daily. If dose is not tolerated, reduce to the previous tolerated dose.

Patients With Hepatic Impairment

For patients with moderate hepatic impairment (Child-Pugh class B), the starting dose is 200 mcg once daily. Increase by 200 mcg once daily at weekly intervals, as

tolerated. Avoid use of UPTRAVI in patients with severe hepatic impairment (Child-Pugh class C).

Co-administration With Moderate CYP2C8 Inhibitors

When co-administered with moderate CYP2C8 inhibitors (eg, clopidogrel, deferasirox and teriflunomide), reduce the dosing of UPTRAVI to once daily. Revert back to twice daily dosing frequency of UPTRAVI when co-administration of moderate CYP2C8 inhibitor is stopped.

Dosage Strengths

UPTRAVI tablet strengths:
200, 400, 600, 800, 1000, 1200, 1400, and 1600 mcg.
Please see full Prescribing Information.

About Pulmonary Arterial Hypertension (PAH)

PAH is a specific form of pulmonary hypertension (PH) that causes the walls of the pulmonary arteries (blood vessels leading from the right side of the heart to the lungs) to become thick and stiff, narrowing the space for blood to flow, and causing an increased blood pressure to develop within the lungs. PAH is a serious, progressive disease with a variety of etiologies and has a major impact on patients' functioning as well as their physical, psychological and social wellbeing. There is currently no cure for PH and it is often fatal.[1,5,6] However, the last decade has seen significant advances in the understanding of the pathophysiology of PAH, transforming the prognosis for PAH patients from symptomatic improvements in exercise tolerance 10 years ago, to delayed disease progression today.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism,

Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. Actelion Pharmaceuticals US, Inc. and Actelion Pharmaceuticals Ltd. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding UPTRAVI® and the SPHERE registry. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com, or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

# # #

[1] Galiè N, Humbert M, et al. Eur Heart J 2016; 37:67-119

[2] Galiè N, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. https://erj.ersjournals.com/content/erj/46/4/903.full.pdf. Accessed March 1, 2021.
[3] UPTRAVI® (selexipag) full prescribing information. Actelion Pharmaceuticals US, Ltd.
[4] Sitbon O, et al. N Engl J Med. 2015;373:2522-2533.
[5] Vachiéry JL, Gaine S. Eur Respir Rev 2012; 21:313-20.
[6] Hoeper MG, Gibbs SR. Eur Respir Rev 2014; 23:450-7.